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10/550,152

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Joacim Elmen

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EXAMINER

VIVLEMORE, TRACY ANN

ART UNIT

PAPER NUMBER

1635

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DELIVERY MODE

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

| | | | |
|------------------------------|--------------------------------------|-------------------------------------|--|
| Office Action Summary | Application No. 10/550,152 | Applicant(s) ELMEN ET AL. | |
| | Examiner Tracy Vivlemore | Art Unit 1635 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 07 May 2010.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 67-97 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 67-97 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date <u>2/14/06, 8/18/09 & 9/16/09</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

This application has been assigned to a different examiner

Election/Restrictions

Applicants' arguments submitted 5/7/10 are persuasive and the requirement for election of species set forth 2/19/10 is withdrawn.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 67-70, 72, 74-77, 79-81 and 91-97 are rejected under 35 U.S.C. 102(e) as being anticipated by Allerson et al. (WO 2004/041889). This application has a priority date of November 5, 2002.

The claims are directed to double-stranded compounds of 12-35 nucleotides comprising at least one locked nucleic acid (LNA) monomer having the structure shown. Particular embodiments recite the size of the compound, the placement of the LNA in

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the sense strand, the antisense strand, or both and recite particular numbers of LNA monomers and their position.

Allerson et al. disclose compositions comprising first and second oligomers capable of hybridizing with each other. In these compositions at least a portion of the first oligomer is complementary to and capable of hybridizing to a selected target nucleic acid and at least one of the first and second oligomers includes at least one polycyclic sugar surrogate. The polycyclic sugar surrogate can be in either or both of the oligomers. The oligomers have 10-40 nucleotides, 18-30 nucleotides or 21-24 nucleotides and can comprise overhangs. One polycyclic sugar surrogate specifically disclosed by Allerson et al. is illustrated at page 15 and in the claims. In this structure X is O, S, NH, or N(R₁), and R₁ is C₁-C₁₂ alkyl or an amino protecting group. This surrogate is identical to that shown in the instant claims. In example 52 Allerson et al. disclose specific siRNA antisense sequences that have LNA nucleotides at the 3' end. Some of these sequences also lack LNA at the 5' ends of the antisense strand.

Thus, Allerson et al. disclose all limitations of and anticipate claims 67-70, 72, 74-77, 79-81 and 91-97.

Claims 67-70, 72, 74-76, 80-82 and 91-97 are rejected under 35 U.S.C. 102(e) as being anticipated by McSwiggen (US 2005/0261212).

The claims are directed to double-stranded compounds of 12-35 nucleotides comprising at least one locked nucleic acid (LNA) monomer having the structure shown. Particular embodiments recite the size of the compound, the placement of the LNA in

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the sense strand, the antisense strand, or both and recite particular numbers of LNA monomers and their position.

McSwiggen discloses siRNAs that are about 19 to about 25 nucleotides in length and can comprise 3'-overhangs. McSwiggen further discloses the siRNAs can comprise chemical modifications in either the sense or antisense strands that impart increased stability and/or nuclease resistance. At paragraph 63 McSwiggen discloses that the siRNAs can comprise one or more (e.g., about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or more) locked nucleic acid nucleotides at the 5'-end, 3'-end, 5' and 3'-end, or any combination thereof. At paragraph 163 McSwiggen discloses that the locked nucleic acid nucleotides are 2', 4'-C methylene bicyclo nucleotide, which is the structure shown in the instant claims.

Thus, McSwiggen discloses all limitations of and anticipates claims 67-70, 72, 74-76, 80-82 and 91-97.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein

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were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 67-97 are rejected under 35 U.S.C. 103(a) as being unpatentable over Allerson et al. as applied to claims 67-70, 72, 74-77, 79-81 and 91-97 above.

The claims are directed to double-stranded compounds of 12-35 nucleotides comprising at least one locked nucleic acid (LNA) monomer having the structure shown. Particular embodiments recite the size of the compound, the placement of the LNA in the sense strand, the antisense strand, or both and recite particular numbers of LNA monomers and their position.

Allerson et al. teach compositions comprising first and second oligomers capable of hybridizing with each other. In these compositions at least a portion of the first oligomer is complementary to and capable of hybridizing to a selected target nucleic acid, and at least one of the first and second oligomers includes at least one polycyclic sugar surrogate. The polycyclic sugar surrogate can be in either or both of the oligomers. The oligomers have 10-40 nucleotides, 18-30 nucleotides or 21-24 nucleotides and can comprise overhangs. One polycyclic sugar surrogate specifically disclosed by Allerson et al. is illustrated at page 15 and in the claims. In this structure X is O, S, NH, or N(R₁), and R₁ is C₁-C₁₂ alkyl or an amino protecting group. This surrogate is identical to that shown in the instant claims. In example 52, Allerson et al.

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teach specific siRNA antisense sequences that have LNA nucleotides at the 3' end.

Some of these sequences also lack LNA at the 5' ends of the antisense strand.

While Allerson et al. explicitly teach that sugar surrogates can be in the sense strand, the antisense strand, or both, they do not exemplify siRNAs having multiple LNA nucleotides in the sense strand or at particular positions as recited in instant claims 71, 78 and 83-90.

At page 68, Allerson et al. teach that their invention includes oligonucleotides that are prepared having enhanced properties compared to native RNA against nucleic acid targets. A target is identified and an oligonucleotide is selected having an effective length and sequence that is complementary to a portion of the target sequence. Each nucleoside of the selected sequence is scrutinized for possible enhancing modifications. A preferred modification would be the replacement of one or more RNA nucleosides with nucleosides that have the same 3'-endo conformational geometry. Such modifications can enhance chemical and nuclease stability relative to native RNA while at the same time being much cheaper and easier to synthesize and/or incorporate into an oligonucleotide. The selected sequence can be further divided into regions and the nucleosides of each region evaluated for enhancing modifications that can be the result of a chimeric configuration. Consideration is also given to the 5'- and 3'-termini as there are often advantageous modifications that can be made to one or more of the terminal nucleosides.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make siRNAs including LNA nucleotides as taught by Allerson et

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al. and to make them with LNA nucleotides of the specific number and placement as recited in the instant claims. Based on the explicit suggestion by Allerson et al. that every position of an oligonucleotides be scrutinized for possible enhancing modifications and that nucleosides like LNA that have 3'-endo conformational geometry are a preferred modification, one of ordinary skill would have reason to make an siRNA with an LNA at the recited positions in order to find the optimum placement for modified nucleotides and would have reasonable expectation of success in making such oligonucleotides because Allerson et al. successfully incorporates LNA nucleotides throughout an oligonucleotide sequence.

Therefore the invention of claims 67-97 would have been obvious, as a whole, at the time the invention was made.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tracy Vivlemore whose telephone number is 571-272-2914. The examiner can normally be reached on Mon-Fri 8:30-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Fereydoun Sajjadi, can be reached on 571-272-3311. The central FAX Number is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

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Status information for unpublished applications is available through Private PAIR only.

For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Tracy Vivlemore
Primary Examiner
Art Unit 1635

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Primary Examiner, Art Unit 1635